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AUTHOR(S):

Nagaki, Aiichiro; Takumi, Masahiro; Tani, Yosuke; Yoshida, Jun-ichi

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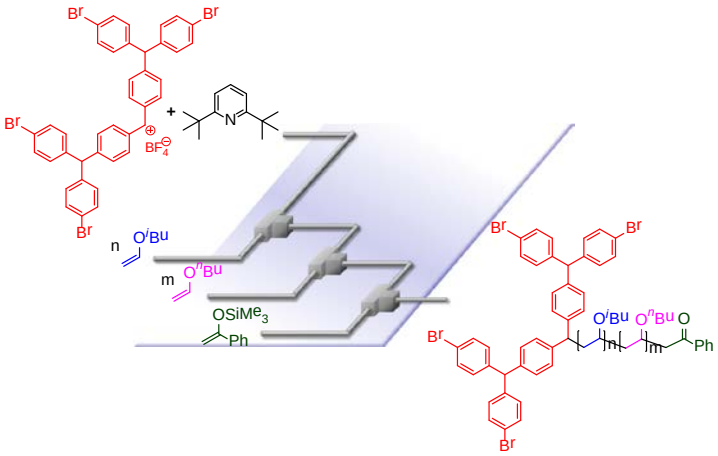
Aiichiro Nagaki, Masahiro Takumi, Yosuke Tani, and Jun-ichi Yoshida*
Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Nishikyo-ku, Kyoto 615-8510, Japan.



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Aiichiro Nagaki, Masahiro Takumi, Yosuke Tani, and Jun-ichi Yoshida*

[a] *Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Nishikyo-ku, Kyoto 615-8510, Japan.*

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ABSTRACT

Cationic polymerization of vinyl ethers initiated by an electrogenerated dendritic diarylcarbenium ion in the presence of 2,6-di-*tert*-butylpyridine was developed using a flow microreactor. The carbocationic polymer end generated by polymerization of isobutyl vinyl ether was effectively trapped by various nucleophiles such as trimethyl(1-phenylvinyloxy)silane and allyltrimethylsilane to give polymers with very narrow molecular weight distribution. The block copolymerization of two vinyl ethers followed by trapping with nucleophiles was successfully accomplished to give structurally well-defined macromolecules.

1. Introduction

Linear-dendritic polymers have emerged as a new important type of macromolecules in materials science,[1] and the ambivalent characteristics of their architecture offer unique/new possibilities for numerous potential applications.[2] Linear-dendritic polymers can be prepared based on three strategies:[3] (1) coupling strategy:[4] coupling of a dendrimer and a functional linear polymer chain, (2) chain-first strategy:[5] the synthesis of a terminally functional polymer chain and the subsequent construction of a dendrimer, and (3) dendron-first strategy:[6] the synthesis of a dendrimer followed by polymerization initiated at the dendrimer. Especially the dendron-first approach is very useful because the dendrimers can be constructed by a convergent synthetic route such as coupling of prefabricated branched units.

We have developed the cation pool method in which organic cations are electrochemically[7] generated and accumulated in solution in the absence of nucleophiles and are used for the reactions with subsequently added nucleophiles.[8] The method has been successfully applied to various organic cations including *N*-acyliminium ions, alkoxycarbenium ions, and diarylcarbenium ions. We have also developed an iterative process for making dendtritic structures based on the cation pool method; a sequence consisting of the electrochemical generation of a diarylcarbenium ion (activation) followed by the reaction with (diphenylmethyl)trimethylsilane as a building block (coupling) is repeated to effect convergent synthesis of dendritic molecules (Figure 1).[9] Notably, dendritic diarylcarbenium ions react with unfunctionalized polystyrenes to give dendronized polymers.[10]

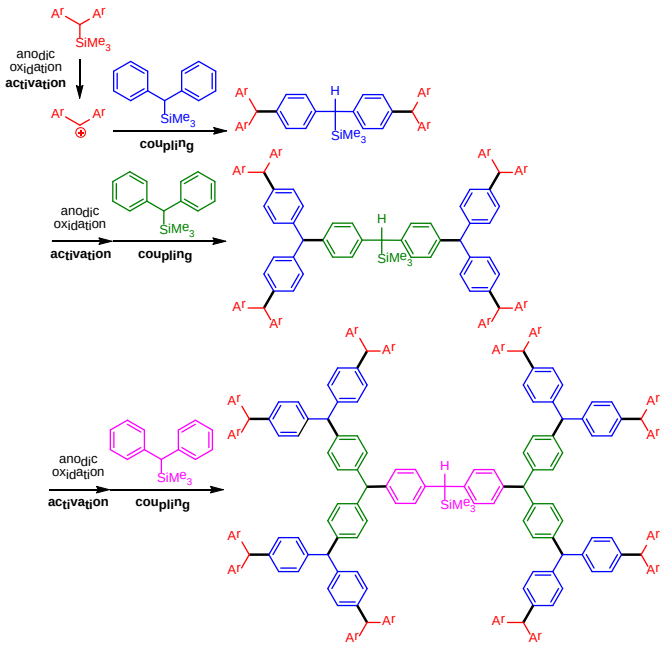


Figure 1. An iterative process for making dendritic structures based on the cation pool method.

* Corresponding author. Tel.: +81-75-383-2726; fax: +81-75-383-2727; e-mail: yoshida@sbchem.kyoto-u.ac.jp

Chemical synthesis in flow microreactors[11,12,13] has attracted a great deal of attention and the applications to polymerization of vinyl monomers have been extensively studied. [14] For example, controlled cationic polymerization[15,16] of vinyl ethers and controlled anionic polymerization[17,18] of styrenes, alkyl methacrylates, and *tert*-butyl acrylate using flow microreactors have been reported in the literature. The molecular weight and the molecular weight distribution can be strictly controlled by virtue of the characteristic features of flow microreactors such as fast mixing, fast heat transfer, and precise residence time control.

Based on these achievements, the following working hypothesis came to our mind. Use of dendritic diarylcarbenium ions as initiators of controlled cationic polymerization in flow microreactors leads to the formation of linear-dendritic polymers bearing living polymer ends which can be trapped with nucleophiles (dendron-first strategy). The method would serve as a powerful and straightforward way of synthesizing structurally well-defined linear-dendritic polymers. However, to the best of our knowledge, such an approach has not yet been reported so far, although studies using ring-opening polymerizations[6c] and living radical polymerizations[6b,6d,6e] have been reported. The concept works, and we report herein the results of this proof-of-principle study.

2. Results and Discussion

Cationic Polymerization of Isobutyl Vinyl Ether Initiated by a Dendritic Diarylcarbenium Ion Pool

We chose to study diarylcarbenium ion **2**[19] as a model of a dendritic initiator of the cationic polymerization. Cation **2** was generated by low temperature electrochemical oxidation of **1**, which has a silyl group as an electroauxiliary[20] for the selective oxidation and peripheral bromo functionalities for future functionalization (Figure 2).

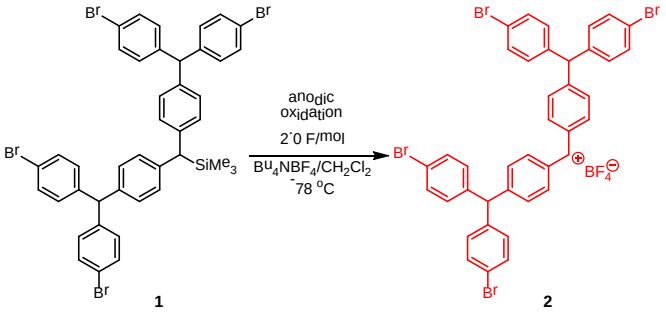


Figure 2. Generation of diarylcarbenium ion **2**.

First, we examined the polymerization of isobutyl vinyl ether using diarylcarbenium ion **2** in a flow microreactor system composed of two T-shaped micromixers (**M1** and **M2**) and two microtube reactors (**R1** and **R2**) (Figure 3). The flow microreactor system was dipped in a cooling bath (-78 °C). A solution of isobutyl vinyl ether (0.50 M in CH_2Cl_2, 10 mL/min) and a solution of **2** (0.050 M in CH_2Cl_2, 5 mL/min) were mixed using **M1** (ϕ = 250 μm). The mixed solution was introduced to **R1** (ϕ = 1000 μm, L = 25 cm), where the polymerization took place. The polymerization was terminated by adding a solution of trimethyl(1-phenylvinyloxy)silane (1.0 M in CH_2Cl_2, 5 mL/min) at **M2** (ϕ = 500 μm) and **R2** (ϕ = 1000 μm, L = 50 cm) to obtain the end-functionalized polymer **3**. When the polymerization was carried out in the presence of a proton trapping agent, the agent was added to a solution of **2** prior to the polymerization.

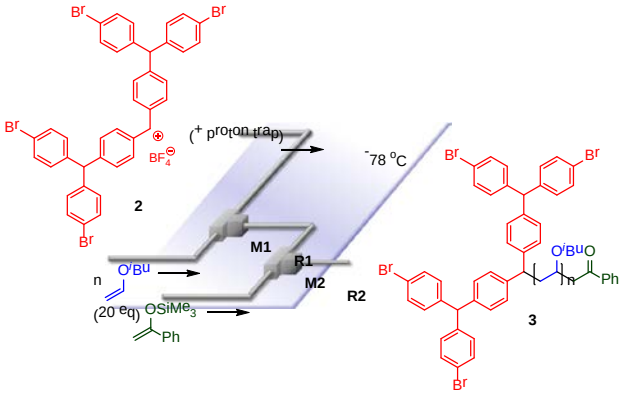
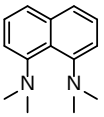
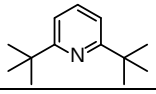


Figure 3. Flow microreactor for cationic polymerization of isobutyl vinyl ether initiated by diarylcarbenium ion **2** in the absence or presence of a proton trapping agent at -78 °C. T-shaped micromixers: **M1** and **M2**. Microtube reactors: **R1** and **R2**.

Figure 4 shows MALDI-TOF mass spectra of the resulting polymers. The polymer produced in the absence of a proton trapping agent is contaminated with a significant amount of the polymer obtained by proton-initiated polymerization (Figure 4 (a)).

Polymerizations in the presence of 1,8-bis(dimethylamino)naphthalene as a proton trapping agent resulted in much low yields of polymer **3**, although **3** was obtained in good yields in the absence of a proton trapping agent (Table 1). In contrast, polymerizations using 2,6-di-*tert*-butylpyridine as a proton trapping agent gave **3** in good yields.

Table 1. Cationic polymerization of isobutyl vinyl ether initiated by diarylcarbenium ion **2** in the absence or presence of a proton trapping agent using a flow microreactor system.

proton trapping agent		M_n[a]	M_w/M_n[a]	yield (%)
-	-	5200	1.08	quant
	0.3 eq	13400	1.10	61
	0.5 eq	12100	1.19	22
	1.0 eq	16100	1.11	6
	0.3 eq	6600	1.06	87
	0.5 eq	8100	1.05	83
	1.0 eq	9000	1.05	90

[a] Polymers were analyzed with size-exclusion chromatography calibrated with polystyrene.

Notably, the use of 2,6-di-*tert*-butylpyridine as a proton trapping agent resulted in a dramatic decrease in the amount of the polymer formed by the proton initiation, although the yield of the polymer was not decreased significantly (Figure 4 (b)). The result indicates that protons, which were presumably generated by the electrolysis, were effectively trapped with 2,6-di-*tert*-butylpyridine. Therefore, the desired polymer **3** with narrow molecular weight distribution (Mw/Mn = 1.05) was obtained, indicating that diarylcarbenium ion **2** worked well as an initiator. In contrast, the polymerization in the presence of 2,6-di-*tert*-butylpyridine (0.5 eq) using a batch macro reactor was examined. The addition of **2** (0.050 M in CH_2Cl_2) and 2,6-di-*tert*-butylpyridine (0.025 M in CH_2Cl_2) (5 mL, 5.0 mL/min) to a solution of isobutyl vinyl ether (10 mL, 0.50 M in CH_2Cl_2) in a glass flask (25 mL) gave the polymer in 84% yield after quenching with trimethyl(1-phenylvinyloxy)silane (1.0 mL, 1.0 M in CH_2Cl_2), but the molecular weight distribution was not

narrow (Mn = 26600, Mw/Mn = 1.45). The reverse addition gave rise to only a slight improvement of the similar molecular weight distribution control (97% yield, Mn = 7560, Mw/Mn = 1.29). The simultaneous addition did not work (96% yield, Mn = 11200, Mw/Mn = 1.59). Thus, it is reasonable to consider that the characteristic features of a flow microreactor system such as fast mixing enables the diarylcarbenium ion intiated polymerization in a highly controlled manner.

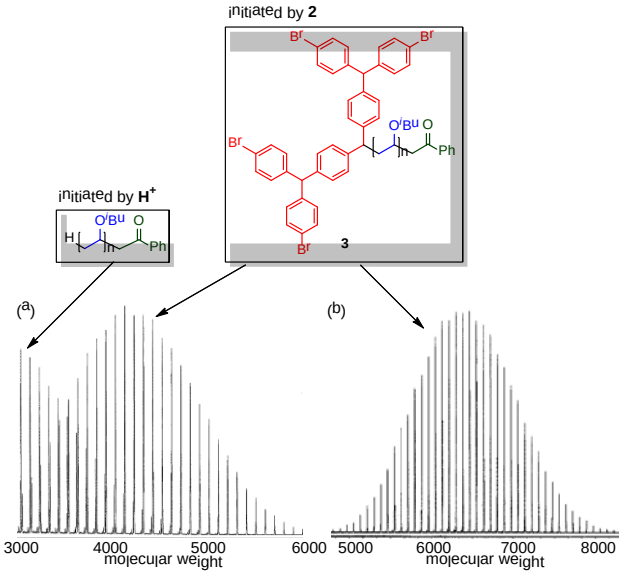


Figure 4. MALDI-TOF mass spectra of the polymers obtained by (a) the polymerization in the absence of a proton trapping agent and (b) the polymerization in the presence of 2,6-di-*tert*-butylpyridine (0.5 eq).

Next, the effect of mixing was examined. Generally, the mixing speed depends on the flow rate and the inner diameter of a micromixer.[21] As shown in Table 2, the molecular weight distribution strongly depends on the flow rate and the inner diameter of micromixer **M1**. The polydispersity index (Mw/Mn) decreased with the increase in the total flow rate in **M1**. The Mw/Mn also decreased with a decrease in the inner diameter of **M1**. The results indicate that extremely fast mixing is responsible for narrow molecular weight distribution (Mw/Mn < 1.10).

Table 2. Effect of mixing for cationic polymerization of isobutyl vinyl ether in the presence of 2,6-di-*tert*-butylpyridine (0.5 eq) initiated by diarylcarbenium ion **2** using a flow microreactor.

inner diameter of **M1** (μm)	total flow rate in **M1** (mL/min)	M_n[a]	M_w/M_n[a]	yield (%)
250	3.0	8600	2.03	55
250	9.0	7000	1.11	99
250	15.0	8100	1.05	83
500	15.0	6100	1.16	95

[a] Polymers were analyzed with size-exclusion chromatography calibrated with polystyrene.

In addition to trimethyl(1-phenylvinyloxy)silane, allyltrimethylsilane was also used as a terminating agent to obtain the end-functionalized polymer **4** in a good yield with narrow molecular weight distribution (Mw/Mn = 1.06). The ^{1}H NMR spectra of polymers **3** and **4** are shown in Figure 5. The two methine protons (H^a) derived from **2** was clearly observed at δ = 5.37 ppm (d, *J* = 2.8 Hz) (for **3** and **4**). The end group such as an aryl group (for **3**: aromatic protons, δ = 7.45, 7.55 and 7.96 ppm) and as an allyl group (for **4**: olefinic protons, δ = 5.01-5.06 and 5.78-5.84 ppm) were observed. The relative intensities of these protons based on the methine proton (H^a) indicate that the carbocationic polymer end was effectively trapped by the added nucleophiles. Therefore, the present method serves as an effective method for synthesis of end functionalized linear-dendritic polymers.

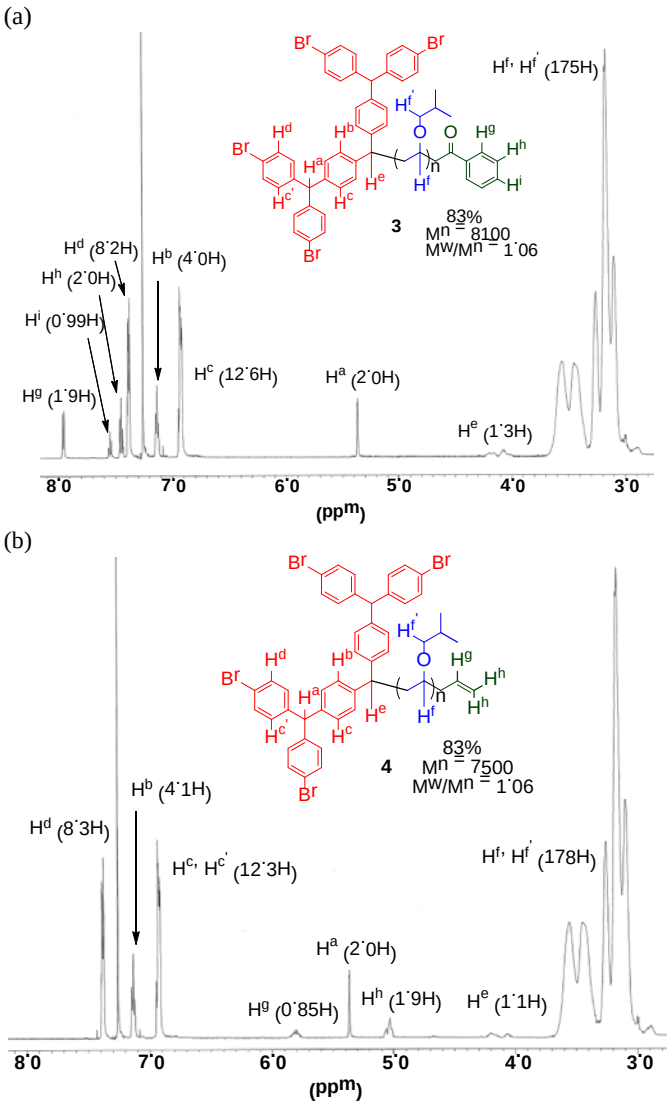


Figure 5. ^{1}H NMR spectra of end-functionalized linear-dendritic polymers; (a) **3** and (b) **4**.

Cationic Block Copolymerization of Vinyl Ethers Initiated by a Diarylcarbenium Ion Pool Using an Integrated Flow Microreactor System

Next, the block copolymerization of isobutyl vinyl ether and *n*-butyl vinyl ether was carried out using an integrated flow microreactor systems consisting of three micromixers (**M1**, **M2**, and **M3**) and three microtube reactors (**R1**, **R2**, and **R3**) shown in Figure 6. A solution of **2** (0.050 M) and 2,6-di-*tert*-butylpyridine (0.025 M) in CH_2Cl_2 (5 mL/min) and a solution of isobutyl vinyl ether (0.50 M in CH_2Cl_2, 10 mL/min) were mixed using **M1** (ϕ = 250 μm). The mixed solution was introduced to **R1**, where the polymerization was carried out. Then, the solution of *n*-butyl vinyl ether (1.0 M in CH_2Cl_2, 5 mL/min) was introduced to **M2** (ϕ = 500 μm), which was connected to **R2** (ϕ = 1000 μm, L = 50

cm (-50 °C) or ϕ = 1000 μm, L = 100 cm (-78 °C)) where the second polymerization took place. The polymerization was terminated by introducing a solution of trimethyl(1-phenylvinyloxy)silane (1.0 M in CH_2Cl_2, 5 mL/min) to **M3** (ϕ = 500 μm) and **R3** (ϕ = 1000 μm, L = 50 cm). GPC traces of the polymers **5** obtained under various conditions are shown in Figure 7.

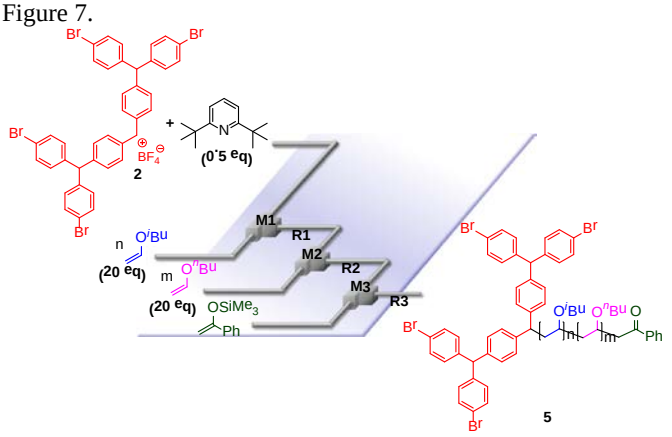


Figure 6. Integrated flow microreactor system for cationic block copolymerization of isobutyl vinyl ether and *n*-butyl vinyl ether initiated by a diarylcarbenium ion **2** in the presence of 2,6-di-*tert*-butylpyridine. T-shaped micromixers: **M1**, **M2**, and **M3**. Microtube reactors: **R1**, **R2**, and **R3**.

The Mn increased when the second monomer solution was added at -50 °C as shown in Figure 7 (a), indicating that the polymerization of the second monomer took place. However, the bimodal molecular weight distribution even with short residence times in **R1** indicates decomposition of the reactive polymer chain end generated by the first polymerization. However, the block copolymerization was successfully carried out without significant decomposition of the living polymer end at -78 °C with a short residence time in **R1** (0.79 s) to obtain **5** in 95% yield with narrow molecular weight distribution (Mw/Mn = 1.08) as shown in Figure 7 (b).

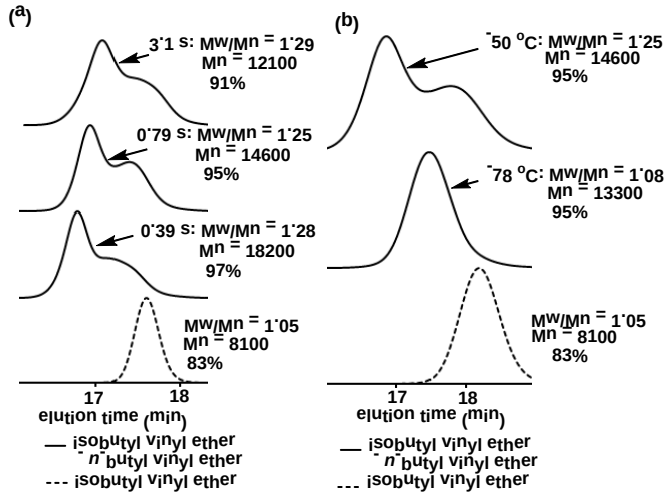


Figure 7. Size exclusion chromatography traces of the cationic block copolymerization of isobutyl vinyl ether and *n*-butyl vinyl ether in the integrated flow microreactor system (a) at -50 °C with varying the residence time in **R1** and (b) with the residence time of 0.79 s in **R1** with varying the temperature.

The ^{1}H NMR (Figure 8) and MALDI-TOF-MS analyses of the resulting polymer **5** revealed that end functional groups were introduced almost quantitatively (See the Supporting Information for details). Notably, the block copolymer **5** bears the bromo groups at the peripheral of the dendritic part, which can be used for further transformations such as Hartwig-Buchwald amination[22].

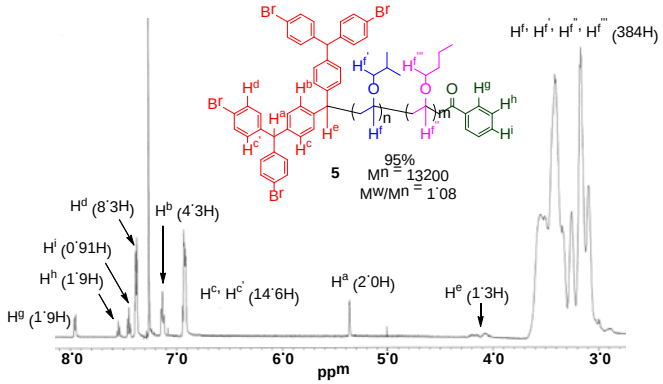


Figure 8. ^{1}H NMR spectrum of end functionalized block copolymers (**5**).

3. Conclusion

In conclusion, controlled cationic polymerization of vinyl ethers initiated by a cation pool of a dendritic diarylcarbenium ion was successfully achieved using the flow microreactor system. Extremely fast mixing is responsible for narrow molecular weight distribution and the polymer end can be used as living reactive species for the subsequent reactions with a nucleophiles and block copolymerization. The observations illustrated here open a new possibility in the synthesis of linear-dendritic polymers. Further applications of the present method are under investigation in our laboratory.

4. Experimental section

General

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on JEOL ECA-600P (^{1}H 600 MHz and ^{13}C 150 MHz). Chemical shifts are recorded using a methine signal of $CHCl_3$ for ^{1}H NMR (7.26 ppm) and ^{13}C NMR (77.0 ppm) unless otherwise noted. MALDI-TOF mass spectra were recorded on Bruker ultraflex. Preparative gel permeation chromatography (GPC) was performed on Japan Analytical Industry LC-918. Dichloromethane was washed with water, distilled from P_2O_5, redistilled from dried K_2CO_3 to remove a trace amount of acid, and stored over molecular sieves 4A. Isobutyl vinyl ether and *n*-butyl vinyl ether were distilled under reduced pressure from CaH_2 twice. Bu_4NBF_4 was dried at 25 °C/1 mmHg for 12 hours. **1** was prepared according to reported procedure[19]. Unless otherwise noted, all materials were obtained from commercial suppliers and were used without further purification. All solutions used for flow reactions were prepared under the argon atmosphere using dry solvents.

Stainless steel (SUS304) T-shaped micromixers with inner diameter of 250 and 500 μm were manufactured by Sanko Seiki Co., Inc. Stainless steel (SUS316) microtube reactors with inner diameter of 1000 μm were purchased from GL Sciences. The micromixers and microtube reactors were connected with stainless steel fittings (GL Sciences, 1/16 OUW). The flow microreactor system was dipped in a cooling bath to control the temperature. The solutions were introduced to the flow microreactor system using Harvard Model 11 syringe pumps equipped with gastight syringes purchased from SGE.

Molecular Weight and Molecular Weight Distribution

The molecular weight (Mn) and molecular weight distribution (Mw/Mn) were determined in THF at 40 °C with a Shodex GPC-101 equipped with two LF-804L columns (Shodex) and an RI detector using a Polystyrene (PolySt) standard sample for calibration.

Electrochemical Generation of the Cation Pool of 2 from 1

The anodic oxidation was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7, ca. 320 mg, dried at 250 °C /1 mmHg for 2.5 h before use) and a platinum plate cathode (20 mm x 10 mm). A 0.3 M solution of **1** (1.55 g, 1.75 mmol) in Bu_4NBF_4/CH_2Cl_2 (35 mL) was placed in the anodic chamber, and a 0.3 M solution of Bu_4NBF_4/CH_2Cl_2 (35 mL) and trifluoromethanesulfonic acid (230 μL, 2.60 mmol) were placed in the cathodic chamber. The constant current electrolysis (40 mA) was carried out at -78 °C with magnetic stirring until 2.0 F/mol of electricity was consumed.

Cationic Polymerization of Isobutyl Vinyl Ether Using Trimethyl(1-phenylvinyloxy)silane as a Terminating Agent in a Flow Microreactor System.

After electrolysis the resulting solution of **2** (6 mL, -78 °C) was transferred to a 20 mL flask at -78 °C, and a proton trapping agent was added. The resulting solution was stirred for 10 min at -78 °C. A flow microreactor system consisting of two T-shaped micromixers (**M1** and **M2**), two microtube reactors (**R1** and **R2**), and three pre-cooling units (**P1** (inner diameter ϕ = 1000 μm, length L = 25 cm), **P2** (ϕ = 1000 μm, L = 50 cm) and **P3** (ϕ = 1000 μm, L = 50 cm)) was used for polymerization. A solution of isobutyl vinyl ether (0.50 M in CH_2Cl_2) and a solution of **2** containing the trapping agent were introduced to **M1**. The mixed solution was passed through **R1** (ϕ = 1000 μm, L = 25 cm) and was introduced to **M2** (ϕ = 500 μm). A solution of trimethyl(1-phenylvinyloxy)silane (1.0 M in CH_2Cl_2) was introduced to **M2** (ϕ = 500 μm), and the resulting solution was passed through **R2** (ϕ = 1000 μm, L = 50 cm). After a steady state was reached, the product solution was collected (10 s) and treated with $^{i}Pr_2NH$. The reactions were carried out by changing the amount of a proton trapping agent, the flow rate, and the inner diameter of **M1**. The solvent was removed under reduced pressure and the residue was filtered through a silica gel column (2 x 3 cm) using Et_2O as an eluent to remove Bu_4NBF_4. The filtrate was concentrated to obtain a polymer product, which was analyzed with size exclusion chromatography. Purified with preparative GPC gave **3**.

Block Copolymerization of Isobutyl Vinyl Ether and *n*-Butyl Vinyl Ether Using Trimethyl(1-phenylvinyloxy)silane as a Terminating Agent in an Integrated Flow Microreactor System

After electrolysis the resulting solution of **2** (6 mL, -78 °C) was transferred to a 20 mL flask at -78 °C and 2,6-di-*tert*-butylpyridine (0.5 equiv based on **1**) was added. The resulting solution was stirred for 10 min at -78 °C. A flow microreactor system consisting of three T-shaped micromixers (**M1**, **M2**, and **M3**), three microtube reactors (**R1**, **R2**, and **R3**), and four pre-cooling units (**P1** (inner diameter ϕ = 1000 μm, length L = 25 cm), **P2** (ϕ = 1000 μm, L = 50 cm), **P3** (ϕ = 1000 μm, L = 50 cm), and **P4** (ϕ = 1000 μm, L = 50 cm)) was used for polymerization. A solution of isobutyl vinyl ether (0.50 M in CH_2Cl_2, 10 mL/min) and a solution of **2** containing 2,6-di-*tert*-butylpyridine (5 mL/min) were introduced to **M1** (250 μm). The mixed solution was passed through **R1** and was introduced to **M2** (ϕ = 500 μm). A solution of *n*-butyl vinyl ether (1.0 M in CH_2Cl_2, 5 mL/min) was introduced to **M2** (ϕ = 500 μm). The mixed solution was passed through **R2** and was introduced to **M3** (ϕ = 500 μm). A solution of trimethyl(1-phenylvinyloxy)silane (1.0 M in CH_2Cl_2, 5 mL/min) was introduced to **M3** (ϕ = 500 μm), and the resulting solution was passed through **R3** (ϕ = 1000 μm, L = 50 cm). After a steady state was reached, the product solution was collected (10 s) and treated with $^{i}Pr_2NH$. The reactions were carried out by changing temperature and the residence time in **R2** and **R3**. The solvent was removed under reduced pressure and the residue was filtered through a silica gel column (2 x 3 cm) using Et_2O as an eluent to remove Bu_4NBF_4. The filtrate was concentrated to obtain a polymer product, which was analyzed with size exclusion chromatography. The polymer product was purified with preparative GPC to obtain **5**.

Supplementary data

Supplementary data related to this article can be found, in the online version, at http://dx.doi.org/

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